UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,882	08/25/2003	Johannes Bartholomaus	785-011444-US(C01)	3177

27384 7590 04/23/2008

NORRIS, MCLAUGHLIN & MARCUS, PA
875 THIRD AVENUE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER
CHOI, FRANK I

ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
04/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/647,882	BARTHOLOMAUS ET AL.	
	Examiner	Art Unit	
	FRANK I. CHOI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 13-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-12 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 9-12, 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dyrsting et al. (US Pat. 6,077,822) in view of WO 00/12067 and EP 0 693 475.

Dyristing et al. disclose that it is common practice in the pharmaceutical industry to use salt forms of drugs, e.g. with physiologically acceptable organic or inorganic acids and basis such as hydrogen chloride and for drugs with amine groups it is feasible to use salts with organic or inorganic acids (Column 1, lines 15-25). It is disclosed that drugs salts with sugar acids, such as monosaccharides, exhibit increased uptake and controlled release properties and that insoluble or poorly soluble drug-sugar acid salts have to found to have a drug release profile that is not dependent on pH in the gastrointestinal tract (Column 1, lines 35-55). It is disclosed that many alkaline drug compounds cause irritation of tissue or mucosa, may also have an unpleasant taste and accordingly they can be administered provided with a polymeric film coating to delay drug release but that is disclosed that such coatings however add to the cost and complexity of formulation (Column 1, lines 28-34).

WO 00/12067 disclose that saccharinate salts of non-alkaloid organic bases provide improved organoleptic properties (page 2).

EP 0 693 475 disclose a 1-phenyl-3-dimethylaminopropane analgesic compounds of formula I, such as (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol that can be converted in a known manner to their salts (Pages 5,15; See English language version - US Pat. 6,344,558, Column 5, lines 25-36, Column 15, lines 40-68).

The prior art discloses the formation of drug salts with sugars. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the (1RS,1RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol salt with sugar. However, the prior art amply suggests the same as the prior art disclose the formulation of drug salts with sugars such as saccharinates. As such, it would have been well within the skill of one of ordinary skill in the art to prepare a (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol salt with a sugar, such as saccharin, with the expectation that the same would be physiologically acceptable and provided improved organoleptic properties.

The Examiner has duly considered the Applicant's arguments but deems them unpersuasive.

The Supreme Court in *KSR International Co. v. Teleflex Inc.*, held the following:

(1) the obviousness analysis need not seek out precise teachings directed to the subject matter of the challenged claim and can take into account the inferences and creative steps that one of ordinary skill in the art would employ;

(2) the obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents;

(3) it is error to look only the problem the patentee was trying to solve-any need or problem known in the filed of endeavor at the time of invention and addressed by the prior art can provide a reason for combining the elements in the manner claimed;

(4) it is error to assume that one of ordinary skill in the art in attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem-common sense teaches that familiar items may have obvious uses beyond their primary purposes, and in many cases one of ordinary skill in the art will be able to fit the teachings of multiple patents together like pieces of a puzzle (one of ordinary skill in the art is not automaton);

(5) it is error to assume that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try". *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396, 1397 (U.S. 2007).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The Applicant provides no evidence that sugar substitutes excludes sugar acids. As indicated above, there is no requirement that Dyrsting et al. disclose the use of the elected

species, (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol. Further, with respect to Rayburn, the Applicant fails to show that the elected species is an alkaloid. The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). Contrary to the Applicant's arguments, the prior art suggests that other than with alkaloids, one of ordinary skill in the art would expect that the combination of active drugs with sugars to form salts of the same would result in reduced solubility. The Applicant argues that formulation of the claimed pharmaceutical salts in to medicaments would be simplified. However, said arguments fails to overcome the rejection herein. See *Pfizer Inc. v. Apotex Inc.*, 82 USPQ2d 1321, 1338 (Fed. Cir. 2007) (Creating a "product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient … to enhance commercial opportunities … is universal—and even common-sensical). Further, the prior art as indicated above, suggest that the sugar salts would simplify complexity and reduce cost in that delayed release coatings would not be necessary due to the controlled release and organoleptic properties of the same. As such, the Applicant has not shown that the simplification of production of medicaments would be unexpected.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the

time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As indicated above, the prior art discloses the preparation of drugs in the form of salts with sugars, including basic drugs containing amine groups which are disclosed in the art to be irritating to the oesophageal mucosa and bad tasting, thus requiring delayed release coatings, and that the sugar salt has controlled release and organoleptic properties. The prior art discloses (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol and that the same can be prepared as a salt. As such, one of ordinary skill in the art would expect a sugar salt of (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol would have controlled release properties and be pleasant tasting without the need of delayed release coatings.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner

maintains a compressed schedule and may be reached Monday, Tuesday, Thursday, Friday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
4/23/08

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616